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LIGAND COUPLING REACTION ON THE PHOSPHORUS ATOM

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Abstract: Phosphine oxides bearing two or three 2-pyridyl groups were found to react with organometallic compounds affording 2,2'-bipyridyl, 2-substituted pyridines and pyridine in substantial yields. Both ligand exchange and ligand coupling appear to take place within the penta-coordinated phosphorus intermediates formed incipiently.

Earlier, we have suggested the concept of ligand coupling within hypervalent intermediates,1) based on our finding that the reaction of optically active 1-phenylethyl 2-pyridyl sulfoxide with either an alkyl or an aryl Grignard reagent gave optically active 2-(1-phenylethyl)pyridine in a quanatitative yield, in which the configuration of 1-phenylethyl group was completely retained.2,3) This coupling reaction is believed to proceed via formation of a σ-sulfurane intermediate upon the nucleophilic attack of the Grignard reagent and subsequent coupling of 2-pyridyl group at an equatorial axis and 1-phenylethyl group at an axial coordinate, after topological transformations. A similar ligand coupling reaction within the intermediary σ-phosphorane is expected. Indeed, there are many examples which belong to this mechanistic type of reaction.1,4-8)

The reaction of triphenylphosphine oxide with organometallic reagents was reported to replace the phenyl group by the other ligand.9) Wittig and Rieber found that tetraphenylphosphonium chloride was formed by the reaction of triphenylphosphine oxide with phenyllithium and the subsequent treatment of the reaction mixture with hydrochloric acid.10) We have now found a new ligand coupling reaction in the treatments of some phosphine oxides bearing two or three 2-pyridyl groups with organometallic compounds.

When tri(2-pyridyl)phosphine oxide 1a was treated with an equivalent of organometallic compound in refluxing THF, 2,2'-bipyridyl 2 was the major product along with 2-substituted pyridine 3 and pyridine 5 as shown in Table. When the reaction was carried out with two equivalents of benzylic Grignard reagent, the yield of 2,2'-bipyridyl was lower than that with an equivalent of the reagent. Since 2,2'-bipyridyl has been found to react easily with the

Table. Reaction of Phosphine Oxides with Organometallic Compounds

Phosphine oxide R^1		Reagent R^2M	Reac. Conditions	Product Yield (%)[a)] 2	3	4	5
1a	2-Py[b)]	MeMgI	THF, reflux, 10h	54	0		15
1a		PhMgBr	THF, reflux, 10h	60	<0.2[c)]		15
1a		PhLi	THF, reflux, 20h	65	<0.2[c)]		29
1a		2-PyLi	THF, reflux, 5h	82			
1a		2-ThiLi[d)]	THF, reflux, 5h	65	0		25
1a		$PhCH_2MgCl$	THF, reflux, 20h	23	9		8
1a		$PhCH_2MgCl$[e)]	THF, reflux, 20h	8	14		9
1a		$p\text{-}MeC_6H_4CH_2MgCl$	THF, reflux, 20h	37	5		7
1a		$p\text{-}MeC_6H_4CH_2MgCl$[e)]	THF, reflux, 30h	2	16		2
1a		$p\text{-}ClC_6H_4CH_2MgCl$	THF, reflux, 20h	31	6		8
1a		$p\text{-}ClC_6H_4CH_2MgCl$[e)]	THF, reflux, 20h	2	17		4
1b	$PhCH_2$	MeMgI	THF, reflux, 20h	41	0	2	6
1b		PhMgBr	THF, r.t., 24h	30	<0.2	0	36
1b		PhLi	THF, reflux, 20h	12	<0.2	11	14
1b		2-PyLi	THF, reflux, 10h	50		13	36
1b		$PhCH_2MgCl$	THF, r.t., 24h	9	37		3
1b		$PhCH_2MgCl$	THF, reflux, 20h	7	46		7
1b		$p\text{-}MeC_6H_4CH_2MgCl$	THF, reflux, 20h	27	34	1	5
1b		$p\text{-}ClC_6H_4CH_2MgCl$	THF, r.t., 24h	7	33	0	0
1c	$p\text{-}MeC_6H_4CH_2$	MeMgI	THF, reflux, 20h	26	0	0	6
1c		PhMgBr	THF, r.t., 24h	45	<0.2[c)]	0	2
1c		PhLi	THF, reflux, 20h	16	<0.2[c)]	11	16
1c		$PhCH_2MgCl$	THF, r.t., 24h	10	48	0	1
1c		$PhCH_2MgCl$	THF, reflux, 20h	3	65	0.4	9
1c		$p\text{-}MeC_6H_4CH_2MgCl$	THF, reflux, 20h	25	39		3
1c		$p\text{-}ClC_6H_4CH_2MgCl$	THF, r.t., 24h	5	38	0	1
1d	Ph	MeMgI	THF, reflux, 10h	35	0	0	9
1d		PhMgBr	THF, r.t., 24h	43	<0.2[c)]		1
1d		PhLi	THF, reflux, 10h	66	<0.2[c)]		16
1d		$PhCH_2MgCl$	THF, reflux, 1h	11	37	0	7
1d		$p\text{-}MeC_6H_4CH_2MgCl$	THF, reflux, 20h	1	54	0	5
1d		$p\text{-}ClC_6H_4CH_2MgCl$	THF, r.t., 24h	10	31	0	2

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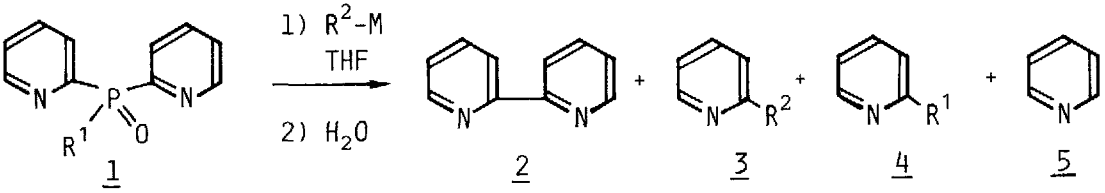
a) Determined by GC analysis. b) 2-Pyridyl. c) Determined by HPLC analysis. d) 2-Thienyllithium. e) Molar ratio; phosphine oxide : R'M = 1 : 2.

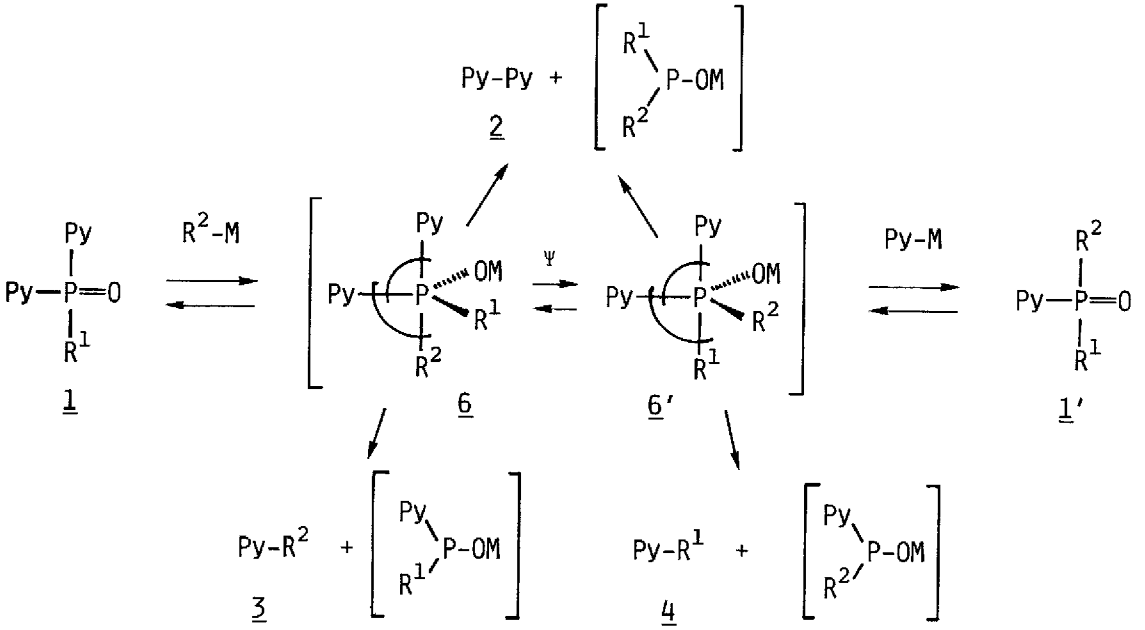
benzylic Grignard reagent, the decrease of the yield was attributed to the consumption of 2,2'-bipyridyl by further reaction with the excess Grignard reagent.

Similarly, concurrent ligand coupling and exchange reactions have been observed in the reaction of other phosphine oxides with organometallic reagents. Those results are also summalized in Table. The reaction with methyl and phenyl Grignard reagents gave predominantly 2,2'-bipyridyl, as shown in Table. Obviously benzylic groups, which are good coupling ligands in the Grignard reaction with 2-pyridyl sulfoxides, were as good ligands as 2-pyridyl to couple with another 2-pyridyl group. Table shows that 2-pyridyl group couples preferentially with the incoming benzylic groups.



Ligand exchange has been observed more pronouncedly with 2-thienyl group, which has been found to be a better leaving ligand than 2-pyridyl group in another experiment.[11)] Thus, treatment of tri(2-thienyl)phosphine oxide 1e with an equivalent of 2-pyridyllithium has afforded mainly thiophene (246%, mol% from 1 mol of 1e), ligand exchange product, along with 2,2'-bipyridyl (21%). This indicates clearly that the initial step of the reaction is ligand exchange on the phosphorous atom, replacing 2-thienyl group by 2-pyridyl group.

The reaction is presumed to proceed through a penta-coordinated phosphorus intermediate 6, formed by the intial attacking of organometallic compound, in which the equatorial 2-pyridyl group couples with either the axial ligand, which may be the incoming group or another 2-pyridyl group, giving 2-substituted pyridines 3 or 2,2'-bipyridyl, respectively, as shown in Scheme.[12)] Formation of pyridine indicates that ligand exchange reaction takes place concurrently. Indeed, small amounts of the ligand exchanged phosphine oxides were detected amomg the reaction mixtures of the phosphine *oxides with organometallic compounds by the use of HPLC. These results* suggest that an alternative route to 2,2'-bipyridyl involves attacking of 2-pyridyl anion formed by the ligand exchange reaction on the original phosphine oxide, as shown previously.[13,14)] The intermediate 6 would pseudoratate to another trigonal bipyramidal structure 6' which would then give another 2-substituted pyridines 4 or 2,2'-bipyridyl.



Scheme

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